



Form 3.54 Division-continuation
program application transmittal form
37 C.F.R. 1.53(b)



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Docket No. POZZ 200004-3-3

IN RE APPLICATION OF: Jose Pozuelo

Prior application: 09/773,336

Mail Stop Patent Application

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

Sir:

This is a request for filing a continuation-in-part application under 37 C.F.R. 1.53(b), of pending prior application U.S. Application Serial No. 09/773,336 filed January 31, 2001 which is a continuation-in-part of Serial No. 09/073,337 filed May 5, 1998.

Inventors: Jose Pozuelo

For: **COMPOSITIONS AND METHODS FOR TREATING PARTICULAR
CHEMICAL ADDICTIONS AND MENTAL ILLNESSES**

1. **Papers Enclosed Which Are Required For Filing Date under 37 CFR
1.53(b) (Regular) or 37 CFR 1.153 (Design) Application**

46 Pages of specification

3 Pages of claims

1 Page of Abstract

 Sheets of drawing

2. A PRELIMINARY AMENDMENT is enclosed.

3. XX Applicant claims small entity status.

4. Request and Certification Under 35 U.S.C. 122(b)(2)(B)(i)

CERTIFICATE OF EXPRESS MAIL

I hereby certify that this **TRANSMITTAL LETTER** and associated papers are being deposited with the United States Postal Service by Express Mail Procedure in an envelope addressed to **Mail Stop Patent Application**, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on January 16, 2004. Express Mailing Label No. EV 34153004 US.

Mary Ann Temesvari
Mary Ann Temesvari

5. ☒ The filing fee is calculated below.

CLAIMS AS FILED IN THE PRIOR APPLICATION LESS ANY CLAIMS CANCELED BY PRELIMINARY AMENDMENT			
Basic Filing Fee (Large Entity)		\$ 385.00	
		No. of Extra Claims Present	Additional Rate
Total Claims	20	0	\$0.00
Indep. Claims	2	0	\$0.00
		Total fee	\$ 385.00

6. ☒ A check in the amount of \$385.00 is enclosed.
7. ☒ The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Account No. 06-0308.
8. ☒ A petition for a three-month extension of time in the parent is also enclosed with a check in the amount of \$475 for the fees.
9. ☐ The prior application is assigned of record to _____, as recorded in the U.S. Patent and Trademark Office.
10. ☒ Enclosed is a Communication to the Examiner.
11. ☐ Please address all future communications to:
- Richard J. Minnich
Fay, Sharpe, Fagan, Minnich & McKee, LLP
1100 Superior Avenue, 7th Floor
Cleveland, OH 44114-2579
12. Please direct all phone calls to Richard J. Minnich or Mark E. Bandy at telephone No. (216)861-5582.

January 16, 2004
Date
Customer No. 27885

Mark E. Bandy
Richard J. Minnich
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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

INVENTOR(S) : Jose Pozuelo

TITLE : COMPOSITIONS AND METHODS
FOR TREATING PARTICULAR
CHEMICAL ADDICTIONS AND
MENTAL ILLNESSES

APPLICATION NO. : Unknown

FILED : Concurrently Herewith

CONFIRMATION NO. : Unknown

EXAMINER : Bennett Celsa (of Parent)

ART UNIT : 1614 (of Parent)

LAST OFFICE ACTION : N/A

ATTORNEY DOCKET NO. : POZZ 200004-3-3
Cleveland, OH 44114
January 16, 2004

COMMUNICATION TO EXAMINER

MAIL STOP PATENT APPLICATION
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This application is a continuation-in-part (CIP) application of U.S. application Serial No. 09/773,336 filed January 31, 2001. The '336 application is being abandoned in favor of this CIP application.

A final Office Action was issued in the '336 application.¹ In that Action, claims 9-13 and 15 were rejected as being obvious over U.S. Patent 4,117,161 to Pozuelo and U.S. Patent 3,810,635 to Pachter et al. All pending claims 9-15 were also

¹ That Action was mailed July 18, 2003.

rejected as being obvious over the noted '161 and '635 patents and further in view of U.S. Patent 5,789,411 to Gooberman and U.S. Patent 5,760,044 to Archer.

It is respectfully submitted that those previous rejections are now moot in view of new claims 1-15 and the presentation of evidence in the form of treatment observations and findings that demonstrate the unexpected and surprising synergy achieved when jointly administering AMPT and Haloperidol as compared to administering either agent alone. The observations and findings have been incorporated into the present application and are found generally at pages 39 to 46. For the Examiner's convenience, the results are summarized below.

The present invention comprises the joint use of AMPT (alpha-methyl-para-tyrosine) and Haloperidol (Haldol), the combination of which has surprisingly been found to be effective for treating addictions to heroin, narcotics, cocaine, amphetamines, alcohol and nicotine, marijuana and mental illnesses such as schizophrenia and manic depressive psychosis.

The use of AMPT for a variety of treatment regimes is noted in the art. The present inventor previously described treatment of patients addicted to narcotics and amphetamines by administering AMPT and a urine alkalinizer in U.S. Patent No. 4,117,161. The '635 patent to Pachter et al. describes combining Haloperidol with a class of narcotic antagonists that are entirely different than AMPT. There is no teaching or suggestion in the '635 patent of combining Haloperidol with AMPT. The '411 patent to Gooberman and the '044 patent to Archer merely note the acknowledged prior use of Naltrexone. Neither of these patents provide any teaching or suggestion of using Naltrexone in combination with AMPT and Haloperidol.

On pages 11-12 of the final Office Action in the parent '336 application, the Examiner invited Applicant to submit evidence as to the benefits and "synergy" of the combined use of agents. Applicant respectfully requests the Examiner to consider the following.

As previously reported in the parent '336 application, a series of treatments for patients with bipolar illness was performed in which AMPT was administered alone to a first group, and AMPT in combination with Haloperidol was administered to a second group. The average length of hospitalization for patients of the first group was 47 days during treatment with AMPT alone. However, for the second group in which patients were treated with the combination of AMPT and

Haloperidol, the average length of hospitalization was reduced to only 12 days! This represents a significant reduction in treatment time and expense.

Another series of tests were conducted in which 16 patients, randomly selected, addicted to heroin, cocaine, or cocaine and alcohol, were assigned to 3 different treatment groups, as follows:

- a) A group of 6 patients, 3 of them addicted to heroin, and another 3 addicted to cocaine plus alcohol, were treated with AMPT alone.
- b) Another group of 6 patients, 3 addicted to heroin and another 3 to cocaine plus alcohol, were treated with Haloperidol alone.
- c) Another group of 4 patients, 2 addicted to heroin and another 2 addicted to cocaine and alcohol, were treated with placebo from the first day of admission.

In the group receiving AMPT alone, the treatment results met only moderate success.

In the group initially receiving Haloperidol alone, after observing the poor to moderate success of Haloperidol alone, AMPT was administered concurrently with further administration of Haloperidol. The beneficial effects of the joint administration of the two agents was striking.

As for the group receiving placebo treatment, no apparent success in treatment was observed.

From these studies, and the results of treatments of more than 300 patients, the following conclusions were drawn.

A) Conclusions Concerning AMPT:

- 1) The combination treatment of AMPT and Haloperidol is extremely more efficient than the treatment with one or the other agent alone.
- 2) The combination treatment comprising AMPT and Haloperidol is able to abolish craving and withdrawal in patients addicted to heroin and cocaine, as demonstrated by the 16 patient study. Similar results were observed in treating many other types of addictions, and some psychiatric conditions, on the almost 300 patients already treated initially with AMPT alone, and in the last 285 patients with the combination of the present invention.
- 3) The treatment with the noted combination results in less suffering; shorter time periods of treatment, be it with hospitalization or not; less financial cost;

and less risk that the patient would leave, renouncing the treatment; and less delay on starting the use of an antagonist, when there is one available for the specific addiction treated.

- 4) The combination treatment is more effective than AMPT alone.

B) Conclusions Concerning Haloperidol:

- 1) The treatment of addiction with Haloperidol alone, as deduced from the 16 patient study, is useless for the treatment of the specific addiction reported.

- 2) Similar results were obtained before in monkeys addicted to narcotics, cocaine, nicotine and for alcohol.

C) Conclusions Regarding Placebo:

From the 16 patient study reported, and a simple blind study, it seems:

- 1) The placebo study is extremely painful for the patients, and results in an unnecessary suffering for the family.

- 2) There exists a high risk of making the patients angry and leaving the treatment or even aggressive thereby causing patients to attack the staff.

Conclusion Summary:

Based upon the findings of the 16 patient study, the present inventor concluded:

- 1) The combination of AMPT and Haloperidol is superior to the effectiveness of each agent alone. This was demonstrated with regard to the addiction reported in the 16 patients and also in the treatment of the many types of addictions and certain psychiatric illnesses that have been treated with the combination of the present invention.

- 2) The results obtained on the above reported study in humans, indicates that the combination treatment is much shorter and much more effective than any one of the combining agents alone.

- 3) It is believed that Haloperidol acts almost immediately by blocking the post-synaptic D₂ dopamine receptor where the increased synthesis of dopamine thus acts and alters the dopamine transporter mechanism. The Haloperidol action is coupled with the AMPT action by inhibiting the tyrosine hydroxylase and, as a

consequence, decreases the dopamine synthesis. A synergistic action occurs when the two agents are administered concurrently.

These observations and findings support a conclusion that the combined administration of AMPT and Haloperidol provides significantly superior results as compared to treatments of either AMPT alone or Haloperidol alone.

In view of this evidence as to the surprising and unexpected results of the joint and concurrent use of AMPT and Haloperidol, it is respectfully submitted that all claims 1-15 are patentable over the cited art.

Respectfully submitted,

FAY, SHARPE, FAGAN,
MINNICH & McKEE, LLP

January 16, 2004
Date

Mark E. Bandy
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Signature <i>Mary Ann Temesvari</i>
Printed Name <i>Mary Ann Temesvari</i>

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

INVENTOR(S) : Jose Pozuelo

TITLE : **COMPOSITIONS AND METHODS
FOR TREATING PARTICULAR
CHEMICAL ADDICTIONS AND
MENTAL ILLNESSES**

APPLICATION NO. : 09/773,336

FILED : January 31, 2001

CONFIRMATION NO. : 4263

EXAMINER : Bennett Celsa

ART UNIT : 1614

LAST OFFICE ACTION : July 18, 2003

ATTORNEY DOCKET NO. : POZZ 200004-3
Cleveland, OH 44114
January 16, 2004

COPY

COMMUNICATION TO EXAMINER

MAIL STOP AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In response to the final Office Action mailed July 18, 2003, in the above-captioned application, Applicant is filing a continuation-in-part (CIP) application from this application.

This application will go abandoned in lieu of the new CIP application.

The initial period for response to the outstanding Office Action expired on October 18, 2003.

Pursuant to 37 C.F.R. 1.136 petition is hereby made for a three-month extension of time up to and including at least January 18, 2004 in which to file the enclosed CIP application. A check in the amount of \$475 is enclosed for the

extension fee. Please charge any additional fees and/or extensions of time which may be required, or credit any overpayment to Deposit Account No. 06-0308.

Respectfully submitted,

FAY, SHARPE, FAGAN,
MINNICH & McKEE, LLP

January 16, 2004
Date

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Pat. Appln., Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Express Mail Label No.: <i>EV 341153004 US</i>
Date <i>January 16, 2004</i>

Signature <i>Mary Ann Temesvari</i>
Printed Name Mary Ann Temesvari